Synthetic Matrices for Stem Cell Growth and Differentiation

Grant Award Details

Synthetic Matrices for Stem Cell Growth and Differentiation

Grant Type: Tools and Technologies I

Grant Number: RT1-01053

Investigator:

Name:	Dennis Clegg
Institution:	University of California, Santa Barbara
Type:	PI

Human Stem Cell Use: Embryonic Stem Cell

Award Value: $599,404

Status: Closed

Progress Reports

Reporting Period: Year 1

View Report

Reporting Period: Year 2

View Report

Reporting Period: NCE

View Report

Grant Application Details

Application Title: Synthetic Matrices for Stem Cell Growth and Differentiation

Public Abstract:

There is a critical need for new technologies to facilitate growth and differentiation of human embryonic stem cells (hESC) using clinically acceptable, animal-free reagents. In particular, most currently used culture conditions are not acceptable for standardized production of clinical grade cell products. We propose to develop novel, well-defined, synthetic extracellular matrices for growth and differentiation of hESC.

Our approach is to first understand how hESC interact with extracellular matrix materials by analyzing candidate adhesive substrate proteins and integrin receptors that mediate attachment, survival, proliferation and differentiation. Biomimetic, synthetic matrices will be developed, with components and strategies informed by our knowledge of fundamental cell biology. We have established an active, interdisciplinary collaboration between experts in cell biology, stem cell culture, peptide chemistry and materials research.

Preliminary data have identified crucial receptors that mediate adhesion and survival of hESC. As proof of concept, novel, biocompatible hydrogel polymers have been developed and analyzed for physical properties, cellular toxicity, and for their ability to support adhesion and growth of hESC. A method for rapid, high throughput screening of candidate hydrogel peptides has been developed using inkjet printing technology.

We propose to develop and test peptide-hydrogels for culture of hESC. Peptides from adhesive extracellular matrix proteins will be screened for their ability to support adhesion, survival, proliferation and differentiation of several hESC lines, including some that are not federally approved. Arrays of candidate materials, using single peptides and combinations of peptides will be arrayed using ink jet printing and assayed in adhesion assays. Larger scale experiments will test adhesive substrates for survival, proliferation, and maintenance of the undifferentiated state.

The proposed experiments, if successful, will address an important unmet need in bringing stem cell therapies to the clinic and provide the foundation for a wide range of fundamental studies.

Statement of Benefit to California:

The State of California, like the rest of the nation, faces immense challenges to its health care system, with soaring medical costs due in part to continuing care of our aging population. The percentage of elderly in California is expected to grow from what was 14 percent in 1990 to 22 percent in 2030. Chronic degenerative diseases such as Alzheimer's disease, Parkinson's disease, age-related macular degeneration, cancer, diabetes, cardiovascular disease, osteoarthritis, and osteoporosis afflict a growing number of individuals in California. Major innovative approaches are now, more than ever, an imperative.

Human embryonic stem cells (hESC) have great potential for the treatment of disease and injury because they are pluripotent in their capability to form most cell types in the body. They will also be of great utility for screening new drug candidates, and for understanding the molecular mechanisms of human development and disease. However, methods used to grow hESC are in their infancy, and scale up for production of clinical grade cells will require further research.

Our proposed research will develop new methods for culture of hESC using synthetic matrices that will be suitable for clinical applications. If successful, this work will be a great benefit to the state by providing useful new technology that addresses a critical need in the field of stem cell research. In addition, it provide new approaches for therapies to treat degenerative conditions that afflict millions of Californians.

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